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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/998,491 | 11/30/2001 | Radmila Mileusnic | 3578-120 | 6361 |

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| EXAMINER | |
|---|---|
| SEHARASEYON, JEGATHEESAN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1647 | |

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/998,491 | MILEUSNIC ET AL. | |
| | Examiner | Art Unit | |
| | Jegatheesan Seharaseyon, Ph.D | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *7,10 and 12-35* is/are pending in the application.

4a) Of the above claim(s) *12,13,15-17,19-21,23-25,27-29,31-33 and 35* is/are withdrawn from consideration.

5)☒ Claim(s) *7 and 10* is/are allowed.

6)☒ Claim(s) *14,18,22,26,30 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. This office action is in response to the amendment and remarks filed on 4/27/06. Claims 7 and 10 have been amended. Therefore, claims 7, 10 and 12-35 are currently pending. Claims 12, 13, 15-17, 19-21, 23-25, 27-29, 31-33 and 35 remain withdrawn. Claims 7,10, 14, 18, 22, 26, 30 and 34 are examined.

2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

3. Applicants declaration filed under Rule 131 has been fully considered.

4. Any objection or rejection of record, which is not expressly repeated in this action, has been overcome by Applicant's response and withdrawn.

5. Claims 7 and 10 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(b), claims 14, 18, 22, 26, 30 and 34, directed to the process of making or using the allowable product, previously withdrawn from consideration as a result of a restriction requirement, is hereby rejoined and fully examined for patentability under 37 CFR 1.104. Claims 13, 15-17, 19-21, 23-25, 27-29, 31-33 and 35, directed to the invention(s) of II and III do not require all the limitations of an allowable product claim, and are NOT been rejoined.

Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, **the restriction requirement between groups I, II and III as set forth in the Office action mailed on 11/4/2003 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claims including all the limitations of an allowable

product claim or rejoined process claim are presented in a continuation or divisional application, such claims may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

***Claim Rejections - 35 USC § 112, first paragraph (new)***

6. Claims 14, 18, 22 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 14, 18, 22 and 26 are drawn to the treatment of a neurodegenerative disease in an animal by administering a pharmaceutical composition comprising a polypeptide SMRER (SEQ ID NO: 4) or RER (SEQ ID NO: 9). Applicants have evaluated the effect of both polypeptides SMRER and RER in early memory using a chicken model (pages 19-23, see also Mileusnic et al. 2000). However, the specification as filed is insufficient to enable one of skilled in the art to practice the claimed invention of treating neurodegenerative disease because the specification has not established whether either or both of the extracellular accumulation of amyloid plaques and intracellular accumulation of tau proteins are the causes or the symptoms of Alzheimer's and related neurodegenerative diseases of Alzheimer type (page 2, lines 7-12). The

specification has not demonstrated that the administration of the SMRER and RER polypeptides will treat neurodegenerative diseases in animals. Applicants have only demonstrated that upon intracranial administration of the SMRER and RER polypeptide to chicken they rescued memory and prevented amnesia induced by Anti-APP antibodies and APP antisense. Although, the chick model appears to be adequate to demonstrate the recovery of memory in chicken it does not appear to represent the pathology of neurodegenerative diseases in animals, for example, no amyloid plaques etc.

If one skilled in the art is not guided as to the pathology of the neurodegenerative disease in general and in specific Alzheimer's disease as discussed above, then the skilled artisan is also not guided as to how to use methods for the treatment, using the compositions comprising these polypeptides. In addition, claims recite the administration of the polypeptide to the animals; Applicants have only demonstrated the intracranial administration in chicks. Applicants have not demonstrated that the polypeptide of the instant invention can be administered by methods other than intracranial injection. For example, will the peptide administered orally reach the brain to affect the memory? Can it be targeted to regions of brain? Applicants have also not provided enabling disclosure for all animals and the ckicken model has not been established as predictive for all animals, including mammals. Since, there is inadequate guidance as to the nature of the invention, it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation to develop methods for the treatment of neurodegenerative disease. In addition, because

there is no working examples provided describing diseases or models with neurodegenerative disease, it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention. In addition, there is no mechanism associated with a neurodegenerative disease recited in the claims. While a mechanism is not required, it can allow extrapolation of enablement to non-exemplified embodiments.

Given the breadth of claims 14, 18, 22 and 26 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for a method of treatment of a neurodegenerative disease in an animal by administering a pharmaceutical composition comprising a polypeptide SMRER (SEQ ID NO: 4) or RER (SEQ ID NO: 9) polypeptides, absent evidence to the contrary.

7. Claims 30 and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for the recovery of memory in chicks by administering a pharmaceutical composition comprising a polypeptide SMRER (SEQ ID NO: 4) or RER (SEQ ID NO: 9), does not reasonably provide enablement for the production of cognitive enhancement in animals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 30 and 34 are drawn to producing a cognitive enhancement effect in an animal by administering a pharmaceutical composition comprising a polypeptide SMRER (SEQ ID NO: 4) or RER (SEQ ID NO: 9). Applicants have evaluated the effect of both polypeptides SMRER and RER in early memory using a chicken model (pages 19-23, see also Mileusnic et al. 2000). The specification has not demonstrated that the administration of the polypeptide will produce cognitive enhancement in all animals. Applicants have demonstrated that upon intracranial administration of the SMRER and RER polypeptide to chicken they rescued memory and prevented amnesia. However, the specification as filed is insufficient to enable one of skilled in the art to practice the claimed invention of producing a cognitive enhancement without an undue amount of experimentation because the specification and the prior art have not demonstrated a cognitive enhancement effect in an animal.

Applicant has not disclosed how to use the claimed invention to produce a cognitive enhancement in an animal. Specification fails to provide guidance to the nexus between memory rescue in chicks to cognitive enhancement in animals. Specifically, the memory model has not been established as predictive of cognitive enhancement. Also, Applicants have not provided enabling disclosure to indicate that the chicken model is predictive in mammals. In addition, there is no guidance provided in choosing the treatment regimen with therapeutically effective amount for administering to the subjects. Pharmaceutical therapies are unpredictable for the following reasons; (1) the proteins may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half life protein; (2)

the protein may otherwise not reach the target area because, for example, the peptides may not be able to cross the blood brain barrier.

Since, there is inadequate guidance as to the nature of the invention, it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation for producing cognitive enhancement by administering the polypeptide of the instant invention. In addition, because the working example provided is limited to intracranial administration of the peptides into chicken it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention.

Given the breadth of claims 30 and 34 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for a method of producing a cognitive enhancement effect in an animal by administering a pharmaceutical composition comprising a polypeptide SMRER (SEQ ID NO: 4) or RER (SEQ ID NO: 9).

8. Claims 7 and 10 are allowable.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

**Contact Information**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JS 07/06

**CHRISTINE J. SAOUD**
**PRIMARY EXAMINER**

Christine J. Saoud